Remarks

Please amend claims 1, 10, 28, and 37. Support for the amendments is found, *inter alia*, at paragraph 27 of the application as filed. Claims 19-27 are canceled.

Claims 1-2, 4-11, 13-20, 22-29, 31-38, and 40-46 stand rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. Claims 1-2, 4-11, 13-20, 22-29, 31-38, and 40-45 were also rejected under 35 U.S.C. 112, first paragraph, as allegedly not being enabled. The presently submitted claims recite an amount of GLP-1, an agonist, analog, or derivative thereof having at least 70% amino acid sequence homology to GLP-1 and that exhibits at least one action of the GLP-1. It is believed that this amendment renders both of these rejections moot.

The fundamental factual inquiry of the written description requirement is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991); *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it"). MPEP 2163.02.

In the present case the rejection asserts that no conserved sequence has been provided by the specification. However, the patent laws do not require a conserved sequence. Rather, the laws require that the specification convey with reasonable clarity to those of ordinary skill in the art that applicant was in possession of the invention. As stated by the Federal Circuit, a compound can be defined by whatever characteristics are sufficient to distinguish it. *Amgen v. Chugai Pharm.* In the present case, the claims recite a method of treating a subject having nephropathy by administering an effective amount of a GLP-1, an agonist, analog, or derivative thereof having at least 70% amino acid sequence homology to GLP-1 and having at least one action of GLP-1. Persons of ordinary skill in the art readily understand which parts of the GLP-1 molecule can be manipulated or substituted to result in a functioning analog or derivative with at least one action of GLP-1. For example, a sequence search illustrates which sub-sequences have been conserved across species and others which have changed and can be manipulated with

substitutions to result in a functioning analog or variant. Indeed, in some cases the analogs exhibit a property superior to that of the original GLP-1 (e.g. exendin-4 has greater stability to Dipeptidyl peptidase IV than GLP-1). Therefore, the present claims do sufficiently distinguish the invention and convey that applicant had possession of the invention as claimed as of the filing date to persons of ordinary skill in the art. By reviewing the conserved and non-conserved sequences persons of ordinary skill would readily arrive at various compounds that have at least 70% amino acid homology to the GLP-1 and have at least one action of GLP-1 by making said substitutions. Thus, the present claims are also enabled because the specification provides sufficient information for the person or ordinary skill to make and use the claimed invention across the scope of the claim.

Claims 1-2, 4-11, 13-20, 22-29, 31038, 40-46, and 47-56 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Coolidge et al. (WO 01/89554) in view of Guitard (US 2001/0016586).

Coolidge discloses treatment of ischemic heart disease (IHD) by administration of GLP-1. Coolidge also discloses that IHD is caused by a decreased oxygen supply to the cardiac tissue that is due to reduced coronary artery blood flow (p. 8, lines 23-26). But Coolidge completely fails to disclose that GLP-1 has any effect that would render it useful in the treatment of nephropathy, end stage renal disease, proteinuria, or glomerulosclerosis. Coolidge also does not disclose how or why GLP-1 treats IHD.

The rejection alleges that Guitard discloses the use of GLP-1 as a hypoglycemic agent in nephropathies, peripheral angiopathies, hypertension, microangiopathic changes, diabetes, and insulin resistance (Office Action mailed 7/25/2007, p. 9).

The Office alleges that the referenced claims are rendered obvious by combining Coolidge and Guitard, further alleging that Coolidge treats ischemic heart disease with GLP-1 and thus inherently treats the same components of the vascular system that are in play in nephropathies (i.e., veins and arteries). The rejection further alleges that the first target in the treatment would have been the endothelium lining these vessels and this is the situation also for nephropathies with can be induced by ischemic events in the kidney. (Office Action mailed 7/25/2007, p. 9).

This rejection is respectfully traversed. The Office has made this combination of references and asserted the rejection based entirely on hindsight reasoning. The rejection arbitrarily and with hindsight selects "veins and arteries" and "endothelium lining" as targets of the treatment, in order to make the rejection. But Coolidge does not disclose GLP-1 as treating "veins and arteries" or "endothelial lining" but rather states that the disclosed methods can be used to "prevent damage associated with ischemia that occurs during Q-wave myocardial infarction," and that the methods "reverse or ameliorate the ischemia-induced damage that occurs during unstable angina and non-Q-wave cardiac necrosis." (p. 6, lines 17-25). Thus, Coolidge suggests a drug action other than that relied upon by the rejection. Therefore, the rationale of the rejection is contradicted by the plain words of the reference, and it is apparent that the rejection can be made only by using hindsight reasoning, which of course is not permitted by the patent laws. (*Cardiac Pacemakers, Inc. v. St. Jude Medical, Inc.*, 381 F.3d 1371 (Fed. Cir. 2004) ("Prior knowledge in the field of the invention must be supported by tangible teachings of reference materials, and the suggestion to combine references must not be derived by hindsight from knowledge of the invention itself").

Neither Coolidge nor Guitard provide any motivation for combining the treatment of ischemic heart disease disclosed by Coolidge with the hypoglycemic agent disclosed by Guitard. No prima facie case of obviousness can be made by merely concluding that Coolidge must be treating "veins and arteries" or their "endothelial lining" to justify a combination with a hypoglycemic agent disclosed by Guitard for use in patients with impaired glucose metabolism. The rejection has combined the references only through use of hindsight reasoning, and by using knowledge disclosed only by Applicant regarding the treatment of nephropathy and other diseases or conditions, or for the improvement of endothelial function. These treatments are not disclosed by the cited art, neither alone or in combination. Thus, no prima facie case of obviousness has been presented.

Nevertheless, no prima facie case of obviousness has been made based on the separate grounds that the combination of references still fails to teach or suggest every limitation of the claims, since neither reference nor the inappropriate combination teaches or suggests the use of GLP-1 in the treatment of any of the claimed diseases or conditions. MPEP 2142.

Closing

In view of the above reconsideration and withdrawal of all rejections is respectfully requested, and that the claims be passed to allowance.

No fee is believed due in association with this response. But if Applicants are in error, the Commissioner is hereby authorized to charge any underpayment or credit any overpayment during the pendency of this application or any patent issuing from this application to Deposit Account No. 010535.

Respectfully submitted,

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